=> s gastric proton pump

12227 GASTRIC 24289 PROTON 251472 PUMP

T.1

11 GASTRIC PROTON PUMP (GASTRIC (W) PROTON (W) PUMP)

=> d 11

5,888,535, Mar. 30, 1999, Methods and compositions for treating gastric disorders using optically pure (-) pantoprazole; Nancy M. Gray, 424/449, 451, 464; 514/338 [IMAGE AVAILABLE]

=> d l1 2-11 ab bib pn

US PAT NO:

5,756,296 [IMAGE AVAILABLE]

L1: 2 of 11

ABSTRACT:

Methods of producing synthetic heteropolymers and multivalent heteropolymeric hybrid structures capable of assembling non-oligonucleotide molecules are provided. These structures are used to direct the assembly of multimolecular complexes. A number of synthetic heteropolymers, multivalent heteropolymeric hybrid structures and multimolecular complexes are also provided.

US PAT NO:

5,756,296 [IMAGE AVAILABLE]

L1: 2 of 11

DATE ISSUED:

May 26, 1998

TITLE:

Nucleotide-directed assembly of bimolecular and

multimolecular drugs and devices

INVENTOR:

Roger S. Cubicciotti, 258 Midland Ave., Montclair, NJ

07042

APPL-NO:

08/575,781 Dec. 22, 1995

DATE FILED: ART-UNIT:

187

PRIM-EXMR:

Bradley L. Sisson

LEGAL-REP:

Law Offices of Jane Massey Licata

US PAT NO:

5,753,265 [IMAGE AVAILABLE]

L1: 3 of 11

ABSTRACT:

A new pharmaceutical multiple unit tableted dosage form containing as active ingredient an acid labile H.sup.+ K.sup.+ -ATPase inhibitor or an alkaline salt thereof or one of its single enantiomers or an alkaline salt thereof, a method for the manufacture of such a formulation, and the method of treatment with such a formulation in medicine.

US PAT NO:

5,753,265 [IMAGE AVAILABLE]

L1: 3 of 11

DATE ISSUED:

May 19, 1998

TITLE:

Multiple unit pharmaceutical preparation

INVENTOR:

Pontus John Arvid Bergstrand, Gothenburg, Sweden

Kurt Ingmar Lovgren, Molndal, Sweden

ASSIGNEE: APPL-NO:

Astra Aktiebolag, Sodertalje, Sweden (foreign corp.)

08/464,774

DATE FILED:

Jun. 22, 1995

ART-UNIT:

152

PRIM-EXMR: ' Thurman K. Page ASST-EXMR: Sharon Howard White & Case LEGAL-REP:

US PAT NO:

5,739,305 [IMAGE AVAILABLE]

L1: 4 of 11

ABSTRACT:

Methods of producing synthetic heteropolymers and multivalent heteropolymeric hybrid structures capable of assembling non-oligonucleotide molecules are provided. These structures are used to direct the assembly of multimolecular complexes. A number of synthetic heteropolymers, multivalent heteropolymeric hybrid structures and multimolecular complexes are also provided.

US PAT NO:

5,739,305 [IMAGE AVAILABLE]

L1: 4 of 11

DATE ISSUED:

Apr. 14, 1998

TITLE:

Nucleotide-directed assembly of bimolecular and

multimolecular drugs and devices

INVENTOR:

Roger S. Cubicciotti, 258 Midland Ave., Montclair, NJ

07042

APPL-NO:

08/487,968 Jun. 7, 1995

DATE FILED: ART-UNIT:

187

PRIM-EXMR:

Bradley L. Sisson

LEGAL-REP:

Law Offices of Jane Massey Licata

US PAT NO:

5,656,739 [IMAGE AVAILABLE]

L1: 5 of 11

ABSTRACT:

Methods of producing synthetic heteropolymers and multivalent heteropolymeric hybrid structures capable of assembling non-oligonucleotide molecules are provided. These structures are used to direct the assembly of multimolecular complexes. A number of synthetic heteropolymers, multivalent heteropolymeric hybrid structures and multimolecular complexes are also provided.

US PAT NO:

5,656,739 [IMAGE AVAILABLE]

L1: 5 of 11

DATE ISSUED:

Aug. 12, 1997

TITLE:

Nucleotide-directed assembly of bimolecular and

multimolecular drugs and devices

INVENTOR:

Roger S. Cubicciotti, 258 Midland Ave., Montclair, NJ

07042

APPL-NO:

08/487,959 Jun. 7, 1995

DATE FILED: ART-UNIT:

187

PRIM-EXMR:

W. Gary Jones Dianne Rees

ASST-EXMR: LEGAL-REP:

Law Offices of Jane Massey Licata

US PAT NO:

5,625,069 [IMAGE AVAILABLE]

L1: 6 of 11

ABSTRACT:

A process of preparing 2-cyano-3,5-dimethyl-4-methoxypyridine. The process includes the steps of: acylating 2-methyl-1-penten-1-alkoxy-3-one to obtain 2-alkoxycarbonyl-3,5-dimethyl-4-pyrone; ammonolyzing 2-alkoxycarbonyl-3,5-dimethyl-4-pyrone to obtain 2-carboxamido-3,5dimethyl-4(1H)-pyridone; methylating 2-carboxamido-3,5-dimethyl-4(1H)pyridone to obtain 2-carboxamido-3,5-dimethyl-4-methoxypyridine; and dehydrating said 2-carboxamido-3,5-dimethyl-4-methoxypyridone to obtain 2-cyano-3,5-dimethyl-4-methoxypyridine.

US PAT NO:

5,625,069 [IMAGE AVAILABLE]

Apr. 29, 1997 DATE ISSUED:

L1: 6 of 11

Process for preparing 2-cyano-3,5-dimethyl-4-TITLE:

methoxypyridine

Shan-Yen Chou, Taipei, tAIWAN, pROVINCE OF CHINA INVENTOR:

Tsai-Mien Huang, Changhua, tAIWAN, pROVINCE OF cHINA Shyh-Fong Chen, Taipei, tAIWAN, pROVINCE OF cHINA

Hao Ku, Taipei, tAIWAN, pROVINCE OF CHINA

Development Center for Biotechnology, China (foreign ASSIGNEE:

> corp.) 08/681,214

APPL-NO: Jul. 22, 1996 DATE FILED:

ART-UNIT: 123

C. Warren Ivy PRIM-EXMR: Garth M. Dahlen ASST-EXMR:

LEGAL-REP: Fish & Richardson P.C.

L1: 7 of 11 5,616,713 [IMAGE AVAILABLE] US PAT NO:

ABSTRACT:

A process of preparing 2-hydroxymethyl-3,5-dimethyl-4-methoxypyridine including the steps of acylating 2-methyl-1-penten-1-alkoxy-3-one to obtain 2-alkoxycarbonyl-3,5-dimethyl-4-pyrone; ammonolyzing 2-alkoxycarbonyl-3,5-dimethyl-4-pyrone to obtain 2-alkoxycarbonyl-3,5dimethyl-4(1H)-pyridone; halogenating 2-alkoxycarbonyl-3,5-dimethyl-4(1H)pyridone to obtain 2-alkoxycarbonyl-4-halo-3,5-dimethylpyridine; methoxylating 2-alkoxycarbonyl-4-halo-3,5-dimethylpyridine to obtain 2-methoxycarbonyl-3,5-dimethyl-4-methoxypyridine; and reducing 2-methoxycarbonyl-3,5-dimethyl-4-methoxypyridine to obtain 2-hydroxymethyl-3,5-dimethyl-4-methoxypyridine.

L1: 7 of 11 5,616,713 [IMAGE AVAILABLE] US PAT NO:

Apr. 1, 1997 DATE ISSUED:

Process of preparing 2-hydroxymethyl-3,5-dimethyl-4-TITLE:

methoxypyridine

Shan-Yen Chou, Taipei, tAIWAN, pROVINCE OF cHINA INVENTOR:

Tsai-Mien Huang, Changhua, tAIWAN, pROVINCE OF CHINA Shyh-Fong Chen, Taipei, tAIWAN, pROVINCE OF CHINA Hao Ku, Taipei, tAIWAN, pROVINCE OF CHINA

Development Center for Biotechnology, Taipei, tAIWAN, ASSIGNEE:

pROVINCE OF cHINA (foreign corp.)

08/681,123 APPL-NO: DATE FILED: Jul. 22, 1996

123 ART-UNIT:

C. Warren Ivy PRIM-EXMR: Garth M. Dahlen ASST-EXMR:

Fish & Richardson P.C. LEGAL-REP:

L1: 8 of 11 5,391,752 [IMAGE AVAILABLE] US PAT NO:

ABSTRACT:

Anti-ulcer agents having a methylsulfinyl bridge between a substituted pyridine moiety and a substituted benzimidazole moiety are prepared by oxidizing the corresponding compounds, having a methylthio bridge, with magnesium monoperoxyphthalate in a suitable solvent. The reaction may be run in an aromatic hydrocarbon solvent, wherein the product may crystallize out of the reaction solution and may be directly isolated by filtration.

L1: 8 of 11 5,391,752 [IMAGE AVAILABLE] US PAT NO:

Feb. 21, 1995 DATE ISSUED:

Process for the preparation of antiulcer agents TITLE:

Robert S. Hoerrner, Scotch Plains, NJ INVENTOR: Joel J. Friedman, East Brunswick, NJ

Joseph S. Amato, Brooklyn, NY Thomas M. Liu, Westfield, NJ

Ichiro Shinkai, Westfield, NJ

Leonard M. Weinstock, Hilton Head, SC

Merck & Co., Inc., Rahway, NJ (U.S. corp.) ASSIGNEE:

08/022,804 APPL-NO:

Feb. 22, 1993 DATE FILED:

ART-UNIT: 123

Jane T. Fan PRIM-EXMR:

Catherine A. Dolan, David A. Muthard, Paul D. Matukaitis LEGAL-REP:

L1: 9 of 11 5,336,503 [IMAGE AVAILABLE] US PAT NO:

ABSTRACT:

A pharmaceutical composition for treating a peptic ulcer, which comprises a myosin light chain kinase inhibitor as an active ingredient and a pharmaceutical additive. The myosin light chain inhibitor reduced the gastric acid secretion and is considered an excellent anti-ulcer agent.

L1: 9 of 11 5,336,503 [IMAGE AVAILABLE] US PAT NO:

Aug. 9, 1994 DATE ISSUED:

Anti-peptic ulcer agent TITLE:

Junichiro Wakasugi, Tokyo, Japan INVENTOR:

Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan (foreign ASSIGNEE:

corp.)

07/861,310 APPL-NO: Mar. 31, 1992 DATE FILED:

152 ART-UNIT:

Thurman K. Page PRIM-EXMR:

William E. Benston, Jr. ASST-EXMR:

Sughrue, Mion, Zinn, Macpeak & Seas LEGAL-REP:

L1: 10 of 11 5,330,982 [IMAGE AVAILABLE] US PAT NO:

ABSTRACT:

The invention relates to the use of a compound which is an antagonist of 5-HT at 5-HT.sub.3 receptors and promotes gastric emptying in conjunction with an H.sup.+ K.sup.+ ATPase inhibitor in the treatment of gastrointestinal disorders.

L1: 10 of 11 5,330,982 [IMAGE AVAILABLE] US PAT NO:

Jul. 19, 1994 DATE ISSUED:

Pharmaceutical composition containing a 5-HT receptor TITLE:

antagonist and an H.sup.+ K.sup.+ Atpase inhibitor and a method of treating gastrointestingal disorders therewith

Michael B. Tyers, Ware, England INVENTOR:

Glaxo Group Limited, London, England (foreign corp.) ASSIGNEE:

07/935,443 APPL-NO: Aug. 25, 1992 DATE FILED:

125 ART-UNIT:

Marianne M. Cintins PRIM-EXMR: William R. A. Jarvis ASST-EXMR:

Bacon & Thomas LEGAL-REP:

L1: 11 of 11 5,149,702 [IMAGE AVAILABLE] US PAT NO:

ABSTRACT:

Provided are cycloheptenopyridine derivatives represented by the general formula ##STR1## [wherein R represents a hydrogen atom or lower alkyl group; R.sup.1 represents a hydrogen atom, halogen atom, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atoms(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or a group-NR.sup.4 R.sup.5 (wherein R.sup.4 and R.sup.5 may be the same or different and each represent a hydrogen atom or lower alkyl group, or R.sup.4 and R.sup.5 mutually combine together

with the nitrogen atom adjacent thereto to form a 5- or 6-membered heterocyclic group); R.sup.2 represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxycarbonyl group, nitro group or amino group; R.sup.3 represents a hydrogen atom, a lower alkyl group, lower alkoxymethyl group, lower alkylcarbonyl group, lower alkoxycarbonyl group, carbamoyl group, lower alkylcarbamoyl group, lower alkylcarbonylmethyl group, lower alkoxycarbonyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminatable in an acid medium or under a physiological condition; n represents 0 or 1; and A represents a methine carbon or nitrogen atom) or their salts. These derivatives and their salts are useful as antiulcer agents.

US PAT NO:

5,149,702 [IMAGE AVAILABLE]

L1: 11 of 11

DATE ISSUED:

Sep. 22, 1992

TITLE:

Cycloheptenopyridine derivatives, process for preparation

thereof and antiulcer agents containing the same

INVENTOR:

Shin-ichi Yamada, Fukushima, Japan

Takao Goto, Koori, Japan Rie Yorita, Fukushima, Japan Eizi Shimanuki, Fukushima, Japan Takaji Yamaguchi, Fukushima, Japan Kentaro Kogi, Shiroishi, Japan Senichi Narita, Tokyo, Japan

ASSIGNEE:

Toa Eiyo Ltd., Tokyo, Japan (foreign corp.)

APPL-NO:

07/618,943 Nov. 27, 1990

DATE FILED: ART-UNIT:

129

PRIM-EXMR: ASST-EXMR:

Carolyn Elmore Scott C. Rand

LEGAL-REP:

Wenderoth, Lind & Ponack

4

ANSWER 1 OF 4 CAPLUS COPYRIGHT 2000 ACS L4GI

$$\begin{array}{c|c}
R^2 & ZR^3 \\
R1 & NCR^4R^5Z^1R
\end{array}$$

Title compds. [I; R = (un)substituted aryl; R1, R2 = H, halo, alkyl; R3 = AB (cyclo)alkyl, (hetero)aryl(alkyl), etc.; R4, R5 = H, alkyl, (hetero)aryl, etc.; Z = 0 or SOO-2; Z1 = bond, alkylene, CO1-2(CH2)m, etc.; m = O-12were prepd. Thus, 4-benzylthioazetidin-2-one (prepn. given) was alkylated by MeCHBrCO2Me and the sapond. product amidated by 4-ClC6H4(CH2)6NH2 to give title compd. II. Data for biol. activity of I were given,.

ΙI

1997:205042 CAPLUS ΑN

126:199444 DN

Preparation of azetidinone derivatives as phospholipase A2 inhibitors TI

Dhanak, Dashyant; Hickey, Deirdre Mary Bernadette; Ife, Robert John; IN Leach, Colin Andrew; Tew, David Graham

Smithkline Beecham Plc, UK; Dhanak, Dashyant; Hickey, Deirdre Mary PABernadette; Ife, Robert John; Leach, Colin Andrew; Tew, David Graham

PCT Int. Appl., 91 pp. SO

CODEN: PIXXD2

DTPatent

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	PATENT NO.					KIND DATE				A.	PPLI	CATI	ο.	DATE						
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			ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,		
			LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,		
			SE,	SG																
		RW:	KE,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,		
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					B2 19990729															
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PRAT					19950701															
		1995-15056																		

Desai

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GB 1995-15206
                      19950725
     GB 1995-16985
                      19950818
     GR 1995-25132
                      19951208
     GB 1996-8650
                      19960426
     GB 1996-8651
                      19960426
     WO 1996-EP2765
                      19960620
OS
     MARPAT 126:199444
     Preparation of azetidinone derivatives as phospholipase A2 inhibitors
ΤI
ΙT
     187813-65-6P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of azetidinone derivs. as phospholipase A2 inhibitors)
RN
     187813-65-6 CAPLUS
     1-Azetidineacetamide, N-[6-(4-chlorophenyl)hexyl]-2-oxo-4-[(2-
CN
     thienylmethyl)sulfinyl]-, (R*,S*)- (9CI) (CA INDEX NAME)
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Relative stereochemistry.

$$\begin{array}{c|c}
O & H \\
N & (CH_2) & 6
\end{array}$$

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2000 ACS GI

Title compds. [I; R1, R2 = H, halo, OH, .omega.-haloalkoxy, alkyl, alkoxy, CF3, .omega.-hydroxyalkoxy, cyano, PhO, phenylsulfonamido, alkoxycarbonylamino, etc.; R3 = R4, (R4-substituted) alkyl, alkoxyalkyl, indanyl, hexahydroindanyl, adamantyl, noradamantyl, norbornyl, etc.; R4 = amino, aryl, furyl, thienyl, pyrrolyl, triazolyl, tetrazolyl, pyridyl, pyrimidinyl, (substituted) cycloalkyl, etc.; R5, R6 = H, halo, alkyl, CF3, cyano, NO2, hydroxylamino, carboxy, (substituted) guanidino, etc.; m = 1-4; with provisos], were prepd. Thus, 5-chloro-1,3-dihydro-3-phenyl-2H-benzimidazol-2-one in DMF was treated with NaH and then 2-methoxy-4-nitrobenzenesulfonyl chloride to give 5-chloro-1,3-dihydro-1-(2-methoxy-4-nitrobenzenesulfonyl)-3-phenyl-2H-benzimidazol-2-one. I inhibited binding of arginine vasopressin to vasopressin V2 receptors with IC50 values of <10-9 M.

Desai

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1995:480317 CAPLUS
ΑN
     122:239703
DN
ΊI
     Preparation of 1-benzenesulfonyl-1,3-dihydro-2H-benzimidazol-2-ones as
     vasopressin and oxytocin antagonists.
ΙŅ
     Di Malta, Alain; Mettefeu, Daniel; Roux, Richard; Garcia, Georges; Nisato,
     Dino; Serradeil-Legal, Claudine
PA
     Sanofi, Fr.
SO
     Eur. Pat. Appl., 62 pp.
     CODEN: EPXXDW
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
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PΙ
     EP 636614
                            19950201
                      Α1
                                           EP 1994-401736
                                                            19940728
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
     FR 2708608
                      A1
                            19950210
                                           FR 1993-9403
                                                            19930730
     FR 2708608
                       В1
                            19951027
                            19950131
     CA 2129214
                       AΑ
                                           CA 1994-2129214
                                                            19940729
     NO 9402835
                            19950131
                                           NO 1994-2835
                      Α
                                                            19940729
     FI 9403571
                      Α
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                                           FI 1994-3571
                                                            19940729
    AU 9468788
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                                           AU 1994-68788
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    AU 679535
                       В2
                            19970703
     ZA 9405655
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                            19950314
                                           ZA 1994-5655
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     ни 67801
                      A2
                                           HU 1994-2238
                                                            19940729
     US 5585394
                            19961217
                      Α
                                           US 1994-282547
                                                            19940729
     CN 1106804
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                            19950816
                                           CN 1994-114901
                                                            19940730
     JP 07215947
                      A2
                            19950815
                                           JP 1994-199080
                                                            19940801
                      19930730
PRAI FR 1993-9403
    MARPAT 122:239703
OS
     Preparation of 1-benzenesulfonyl-1,3-dihydro-2H-benzimidazol-2-ones as
ΤI
     vasopressin and oxytocin antagonists.
ΙT
    162138-94-5P
    RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
    preparation); THU (Therapeutic use); BIOL (Biological study); PREP
```

(Preparation); USES (Uses)

(prepn. of 1-benzenesulfonyl-1,3-dihydro-2H-benzimidazol-2-ones as vasopressin and oxytocin antagonists)

162138-94-5 CAPLUS RN

2H-Benzimidazol-2-one, 3-cyclohexyl-1-[[4-(2,5-dihydro-1H-pyrrol-1-yl)-2-CN methoxyphenyl]sulfonyl]-5-ethoxy-1,3-dihydro- (9CI) (CA INDEX NAME)

L4ANSWER 3 OF 4 CAPLUS COPYRIGHT 2000 ACS GΙ

The title compds. [I; R1 = lower alkoxy; B = N(O), N; R3 = lower alkyl; A AB = lower alkylene; R2 = 5- to 13-membered ring (un)satd. mono-, di-, or tricyclic heterocyclyl having $1-4\ \mathrm{N}$ atoms and optionally substituted with oxo group, XR4, NH2, NHCOR6; X = O, S, SO SO2; R4 = Ph optionally having a substituent selected from OH, phenyl-lower alkoxy, or halo, 5- to 10-membered ring unsatd. heterocyclyl contg. 1-3 atoms selected from N, O, and S and optionally substituted with lower alkyl or Ph; R6 = lower alkyl, Ph optionally having lower alkyl which may be substituted with 1-3 halogen atoms, phenyl-lower alkenyl optionally having lower alkoxy group on the Ph ring] are prepd. These pyrazine derivs. I are useful for the treatment or prevention of superoxide (O2-)-related diseases such as autoimmune diseases (e.g. rheumatism), arteriosclerosis, ischemic heart disease or brain disorder, liver or kidney failure, and nephritis. Thus, 0.15 g NaOMe was added to a soln. of 0.20 g 3-mercapto-1,2,4-triazole and 0.44 g dihydropyrazinone oxide [II; R2A = BrCH2] in anhyd. MeOH and the resultant mixt. was stirred at room temp. for 13 h followed filtration of pptd. crystals and recrystn. from MeOH to give 0.34 g title compd. II(R2A = Q). II showed IC50 of <0.3 .times. 10-5 g/mL for inhibiting the prodn. of H202 in rat neutrophil leukocyte of abdominal cavity. II (R2A = benzothiazol-2-ylsulfonyl) inhibited the mineral oil-stimulated prodn. of macrophage in guinea pig abdominal cavity with IC50 of 0.3 .times. 10-5g/mL. A tablet formulation contg. II (R2A = Q1) was given.

AN 1994:630792 CAPLUS

DN 121:230792

TI Preparation of 1,2-dihydropyrazin-2-one derivatives as superoxide inhibitors and having antiproteinuria effect against Masugi nephritis

IN Tone, Hitoshi; Tamura, Katsumi; Sato, Hideaki; Morisue, Masatoshi; Myazaki, Toshiki; Nakano, Yoshimasa

PA Otsuka Pharma Co Ltd, Japan

SO Jpn. Kokai Tokkyo Koho, 37 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 06135946 A2 19940517 JP 1992-333428 19921030

PI JP 06135946 OS MARPAT 121:230792

TI Preparation of 1,2-dihydropyrazin-2-one derivatives as superoxide inhibitors and having antiproteinuria effect against Masugi nephritis

IT 158314-94-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as superoxide inhibitor)

RN 158314-94-4 CAPLUS

CN 2(1H)-Pyrazinone, 6-[(2-benzothiazolylsulfonyl)methyl]-5-methoxy-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \cdot & \circ & \circ & H & \circ \\ \hline \cdot & S & S - CH_2 & H & \circ \\ \hline \cdot & S & O & MeO & N & Bu-i \end{array}$$

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2000 ACS GI

The title compds. (I; R1, R2 = H, halo, alkyl, alkoxy, etc., R1R2 = benzo; R3, R5 = H, alkyl, alkoxy, alkoxycarbonyl, haloalkoxy; R4 = H, alkyl, aralkyl, etc.; X = S, SO), effective antiulcer agents, are prepd. 2-Mercaptobenzimidazole (600 mg) and 920 mg pyrazole salt II were added to a soln. of 85% NaOH in MeOH with stirring at room temp. to give 311 mg sulfide I (R1 = R2 = R4 = H, R3 = R5 = Me, X = S), which (258 mg) was oxidized with m-ClC6H4CO2OH in CH2Cl2 at -60.degree. to -70.degree. to give 128 mg sulfoxide I (R1 = R2 = R4 = H, R3 = R5 = Me, X = SO), (III). III inhibited stress-induced ulcer formation by 82% at 10 mg/kg p.o. in rats, vs. 72% with cimetidine at 100 mg/kg. A tablet formulation was prepd. from III 20, lactose 100, corn starch 36, cryst. cellulose 30, CM-cellulose Ca 10, and Mg stearate 4 g. Also prepd. were 110 I, 2 formulations, and 12 pyrazole intermediates.

AN 1989:594760 CAPLUS

DN 111:194760

TI Preparation and formulation of (pyrazolylmethylthio)benzimidazoles as antiulcer agents

IN Tanaka, Masaaki; Shinozaki, Katsuo; Niwa, Seiichi; Ogura, Kuniyoshi; Tanaka, Yoshiaki; Shimizu, Masao; Arai, Heihachiro

PA Zeria Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 56 pp. CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PΙ

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63313784	A2	19881221	JP 1987-256216	19871013

PRAI JP 1987-55429 19870312

OS MARPAT 111:194760

TI Preparation and formulation of (pyrazolylmethylthio)benzimidazoles as antiulcer agents

IT 123452-47-1P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as antiulcer agent)

RN 123452-47-1 CAPLUS

CN 1H-Benzimidazole, 2-[[(3,5-dimethyl-4-nitro-1H-pyrazol-1-yl)methyl]sulfinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \cdot & H & O \\ \hline \cdot & | & | & \\ \hline \cdot & | & | & \\ \hline & N & S- CH_2 - N & Me \\ \hline & Me & NO_2 \\ \end{array}$$

8945425 Page 1

L2 ANSWER 1 OF 74 CAPLUS COPYRIGHT 2000 ACS

Gastroesophageal reflux disease (GERD) is a chronic condition, with 50-80% AΒ of patients experiencing recurrence within one year of completing initial treatment. In patients with erosive GERD, proton-pump inhibitors (PPI) provide faster healing and symptom relief than do H2-receptor antagonists and have become the treatment of choice. Rabeprazole is a new PPI with demonstrated efficacy in both the acute and maintenance treatment of erosive GERD. The primary objective was to compare efficacy and tolerability of rabeprazole and omeprazole in preventing relapse of healed erosive GERD. Secondary objectives included comparison of efficacy in preventing GERD relapse symptoms and in maintaining quality of life. In this multicenter, double-blind, parallel-group study, 243 patients with healed erosive GERD were randomized to receive rabeprazole 10 mg once daily in the morning (QAM) (N = 82); rabeprazole 20 mg QAM (N = 78); or omeprazole 20 mg QAM (N = 83). Endoscopies were performed at weeks 13, 26, 39 (if clin. indicated), and 52, or when symptoms suggested recurrence. Corpus biopsies were performed at each endoscopy, and antral biopsies were performed at study entry and exit. Rabeprazole 10 mg and 20 mg QAM were equiv. to omeprazole 20 mg QAM for all efficacy parameters. At week 52, relapse rates in the intent-to-treat populations were 5%, 4%, and 5% for rabeprazole 10 mg and 20 mg and omeprazole 20 mg, resp. All treatments were well tolerated. conclusion, both rabeprazole 10 mg and 20 mg QAM are equiv. to omeprazole 20 mg QAM in preventing recurrence of erosive GERD.

AN 2000:324950 CAPLUS

DN 132:329729

Rabeprazole versus omeprazole in preventing relapse of erosive or ulcerative gastroesophageal reflux disease: A double-blind, multicenter, European trial

AU Thjodleifsson, Bjarni; Beker, Johannes A.; Dekkers, Cornelius; Bjaaland, Tone; Finnegan, Victoria; Humphries, Thomas J.

CS National Hospital of Iceland, Reykjavik, Iceland

SO Dig. Dis. Sci. (2000), 45(5), 845-853 CODEN: DDSCDJ; ISSN: 0163-2116

Kluwer Academic/Plenum Publishers

DT Journal

LA English

RE.CNT 30

RE

PB

- (1) Besancon, M; J Biol Chem 1997, V272, P22438 CAPLUS
- (5) Cloud, M; Dig Dis Sci 1998, V43, P993 CAPLUS
- (6) Dekkers, C; Aliment Pharmacol Ther 1998, V12, P789 CAPLUS
- (7) Dekkers, C; Aliment Pharmacol Ther 1999, V13, P179 CAPLUS
- (8) Dekkers, C; Aliment Pharmacol Ther 1999, V13, P49 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L2 ANSWER 2 OF 74 CAPLUS COPYRIGHT 2000 ACS
- Objective: This paper examines the clin. pharmacol. of the **proton**-pump inhibitors (PPIs) and briefly reviews some
 comparative studies of these agents. Background: PPIs have emerged as the
 treatment of choice for acid-related diseases, including gastroesophageal
 reflux disease (GERD) and peptic ulcer disease. Although these
 drugs-omeprazole, lansoprazole, pantoprazole, and rabeprazole-share a
 common structure (all are substituted benzimidazoles) and mode of action
 (inhibition of H+,K+-ATPase [ATPase]), each differs
 somewhat in its clin. pharmacol. Results: In comparative clin. trials
 found in MEDLINE, PPIs administered once daily produced endoscopic
 evidence of healing in >90% of patients with duodenal ulcer after 4 wk of
 treatment, in >90% of those with gastric ulcer after 6 wk of treatment,
 and in >90% of those with ulcerative or erosive GERD after 8 wk of
 treatment. Maintenance therapy with daily doses of a PPI has been shown

to be an effective means of preventing GERD relapse. PPIs also inhibit the growth of Helicobacter pylori, now recognized as an important factor in peptic ulcer disease, and, when administered in combination with antibiotics, provide the best treatment for eradication of the bacterium. Rabeprazole has a more rapid onset of H+,K+-ATPase inhibition than the other PPIs and, compared with omeprazole, a greater effect on intragastric pH after the first dose. Omeprazole and lansoprazole have a greater potential for drug-drug interactions than do pantoprazole and rabeprazole. Conclusion: Although the individual PPIs have similar efficacy in many cases, differences between them should be considered when choosing a treatment regimen.

AN 2000:287997 CAPLUS

TI The proton-pump inhibitors: similarities and differences

AU Horn, John

CS University of Washington School of Pharmacy, Seattle, WA, USA

SO Clin. Ther. (2000), 22(3), 266-280 CODEN: CLTHDG; ISSN: 0149-2918

PB Excerpta Medica, Inc.

DT Journal

LA English

RE.CNT 52

RE

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- (8) Chu, K; Am J Gastroenterol 1998, V93, P1436 CAPLUS
- (9) Dekkers, C; Aliment Pharmacol Ther 1998, V12, P789 CAPLUS
- (10) Dekkers, C; Aliment Pharmacol Ther 1999, V13, P179 CAPLUS
- (11) Dekkers, C; Aliment Pharmacol Ther 1999, V13, P49 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L2 ANSWER 3 OF 74 CAPLUS COPYRIGHT 2000 ACS
- Lansoprazole(L), pantoprazole (P), rabeprazole and RO-18-5364 (RO) are new AΒ benzimidazole derivs. which rival omeprazole (O) as proton pump inhibitors (PPIs) for treatment of ulcer disease. In this study, we compared the effects of these compds. on acid secretion and detd. their relative potencies in relation to their effect on [14C]-aminopyrine (AP) accumulation in isolated gastric glands. Inhibition of AP (1.2 .mu.Ci.bul.mL-1) accumulation was measured in rabbit isolated gastric glands. DbcAMP (1 mmol; stimulant of acid secretion) and Ro 20-1724 (0.1 mmol; a phosphodiasterase inhibitor) were added to the Eppendorf tubes contg. the PPIs and AP and dose-response curves were done for each drug after incubating for 5, 10 and 20 min at 37 .degree.C and AP accumulation was detd. using a scintillation counter. All the PPIs significantly (P < 0.001) inhibited acid secretion as demonstrated by the inhibition of AP accumulation in the isolated gastric glands. Min. inhibition occurred at a concn. of 0.001 .mu.mol for lansoprazole and omeprazole, 0.01 .mu.mol for rabeprazole and RO 18-5364 and 0.02 .mu.mol for pantoprazole. No differences were obsd. between PPIs with regards to the max. inhibition they produce. When expressed as a percentage inhibition of control at 10-min incubation and at concns. of 1 .mu.mol, L showed 85.6 .+-. 0.5, O 87 .+-. 0.5, P 83.2 .+-. 1.1, R 86.4 .+-. 1.1 and RO 87.8 .+-. 1.9 inhibition resp. When comparing the IC50 values, their relative potencies were different. Maximum potency was shown by L (0.007).mu.mol) > O (0.012 .mu.mol) > R (0.018 .mu.mol) > RO (0.034 .mu.mol) > P(0.050 .mu.mol). All the new PPIs showed different potencies as inhibitors of acid secretion as evident from their IC50s. Extensive ulcer healing trials demonstrated comparable efficacy with a no. of studies indicating that symptoms relief are more rapid with P and L, while in this study L appeared to be the most potent in inhibiting AP accumulation in
- the isolated gastric glands. AN 2000:262857 CAPLUS
- TI Comparison of five antisecretory agents acting via gastric H+/K+-
- AU Bastaki, Salim M. A.; Chandranath, Irwin; Garner, Andrew
- CS Department of Pharmacology, UAE University, Al Ain, United Arab Emirates
- SO J. Physiol. (Paris) (2000), 94(1), 19-23

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CODEN: JHYSEM; ISSN: 0928-4257
     Editions Scientifiques et Medicales Elsevier
PB
DT
     Journal
LA
    English
RE.CNT 18
RE
(9) Im, W; Biochem Biophys Res Commun 1985, V126, P78 CAPLUS
(10) Konturek, S; Gastroenterology 1984, V86, P71 CAPLUS
(11) Kromer, W; J Pharmacol Exp Ther 1990, V254, P129 CAPLUS
(13) Larsson, H; Gastroenterology 1983, V85, P900 CAPLUS
(14) Morii, M; Biochem Pharmacol 1990, V39, P661 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 4 OF 74 CAPLUS COPYRIGHT 2000 ACS
L2
    A method for the treatment of infectious gastrointestinal ulcer disease or
AB
     infectious gastritis disease of microbially infected gastrointestinal
     tissue in a mammal involves administration of an antimicrobial amt. of an
     antimicrobial medicament which is cell wall constituent-inactivating by
     chem. reaction with cell wall constituents, endotoxin non-releasing,
     exotoxin-inactivating, or a combination thereof.
     2000:190931 CAPLUS
ΑN
     132:231932
DN
     Taurolidine and/or taurultam against infectious ulcer or gastritis
TI
     Pfirrmann, Rolf
ΙN
     Ed Geistlich Sohne A.-G. fur Chemische Industrie, Switz.; Pett,
PΑ
     Christopher
SO
     PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT
     Patent
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     English
FAN.CNT 1
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             PT, SE
PRAI US 1998-154451
                      19980916
     US 1999-316115
                    19990520
RE.CNT
(1) Blenkharn, J; Surgical Research Communications 1987, P152
(2) Pett, C; WO 9934805 A 1999
(3) Pfirrmann, R; US 5210083 A 1993
(4) Pfirrmann, R; US 5593665 A 1997
     ANSWER 5 OF 74 CAPLUS COPYRIGHT 2000 ACS
L2
     Proton pump inhibitors (PPIs) block gastric
AB
     acid secretion and may increase serum gastrin concn. The aim of this
     study was to det. whether fasting serum gastrin concn. predicts gastric
     acid suppression in patients on PPI therapy. Ambulatory pH monitoring
     with one pH probe in the distal esophagus and a second probe in the
     stomach was performed in patients with persistent symptoms of GERD despite
     PPI treatment. Upon completion of pH monitoring, blood was drawn for
     measurement of fasting serum gastrin concn. In all, 51 patients were
     studied: 26 on PPIs, 1 on H2-receptor antagonists, and 24 off acid
     suppression. Fasting serum gastrin correlated inversely with percent time
     of gastric pH <4 for all patients (r = -0.553) and for the subgroup of 26
     patients on PPIs (r = -0.435). In patients on PPIs, an elevated gastrin (.gtoreq.100 pg/mL) was assocd. with gastric pH <4 for 25% of the time
     compared to 54% when the gastrin was normal. Therapeutic gastric acid
     suppression (gastric pH <4 for <50% of time) was present in 6 of 7 (86%)
     patients with an elevated fasting serum gastrin, compared with only 8 of
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19 (42%) patients with a normal serum gastrin. In conclusion, there is a significant inverse correlation between the fasting serum gastrin concn. and gastric acid profile in patients with GERD. An elevated fasting serum

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gastrin concn. while on PPI therapy suggests that gastric acid secretion
     is adequately suppressed.
     2000:162374 CAPLUS
ĂΝ
     132:303711
DN
     Does fasting serum gastrin predict gastric acid suppression in patients on
ΤI
    proton-pump inhibitors?
     Bonapace, Eugene S.; Fisher, Robert S.; Parkman, Henry P.
ΑU
     Temple University School of Medicine, Philadelphia, PA, USA
CS
     Dig. Dis. Sci. (2000), 45(1), 34-39
SO
     CODEN: DDSCDJ; ISSN: 0163-2116
     Kluwer Academic/Plenum Publishers
PΒ
     Journal
DT
    English
LA
RE.CNT 19
RE
(1) Banerjee, S; Aliment Pharmacol Ther 1995, V9, P507 CAPLUS
(4) Fimmel, C; Gastroenterology 1985, V88, P1842 CAPLUS
(5) Fisher, R; Am J Gastroenterol 1997, V92, P263 CAPLUS
(9) Kuo, B; Am J Gastroenterol 1996, V91, P1532 CAPLUS
(11) Leite, L; Am J Gastroenterol 1996, V91, P1527 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
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Ι

Many 8-[(2-benzimidazolyl)sulfinyl]-5,6,7,8-tetrahydroquinolines were synthesized and examd. for their (H+ + K+) ATPase ATPase
-inhibitory and antisecretory activities. These sulfinyl compds. could be considered to be rigid analogs of the 2-[(2-pyridyl)methylsulfinyl]benzimi dazole class of antisecretory agents. All the compds. tested were potent inhibitors of (H+ + K+)ATPase. Most of the compds. also inhibited histamine-induced gastric acid secretion in rats. Among them, 8-[(5-fluoro-2-benzimidazolyl)sulfinyl]-3-methyl-5,6,7,8-tetrahydroquinoline (I) was found to have the most potent activity. The structure-activity relationships are discussed.

AN 1990:77040 CAPLUS

DN 112:77040

TI Studies on proton pump inhibitors. I.

Synthesis of 8-[(2-benzimidazolyl)sulfinyl]-5,6,7,8-tetrahydroquinolines
and related compounds

AU Uchida, Minoru; Morita, Seiji; Chihiro, Masatoshi; Kanbe, Toshimi; Yamasaki, Katsuya; Yabuuchi, Youichi; Nakagawa, Kazuyuki

CS Tokushima Res. Inst., Otsuka Pharm. Co., Ltd., Tokushima, 771-01, Japan

SO Chem. Pharm. Bull. (1989), 37(6), 1517-23 CODEN: CPBTAL; ISSN: 0009-2363

DT Journal

LA English

OS CASREACT 112:77040

L2 ANSWER 72 OF 74 CAPLUS COPYRIGHT 2000 ACS

The choice of the stalk cell differentiation pathway in Dictyostelium is AB promoted by an endogenous substance, DIF-1, which is 1-(3,5-dchloro-2,6dihydroxy-4-methoxyphenyl)-1-hexanone. It is also favored by weak acids and two inhibitors of the plasma membrane proton pumps of fungi and plants, diethylstilbestrol (DES) and zearalenone, and antagonized by ammonia and other weak bases, which promote spore differentiation. It has been proposed that the choice of differentiation pathway is regulated by intracellular pH and that DIF-1 itself is a plasma membrane proton pump inhibitor. Expts. showing that DIF-1 is not a plasma membrane proton pump inhibitor are reported. Diethylstilbestrol and zearalenone did inhibit the plasma membrane proton pump of Dictyostelium, and there was an excellent qual. and quant. correlation between the inhibitory activity of these agents, and of a no. of other substances, and their ability to divert differentiation from the spore to the stalk pathway. Thus, inhibition of the plasma membrane proton pump does shift the choice of differentiation pathway in Dictyostelium towards the stalk pathway, but DIF does not act by this route. A model is proposed for the actions of DIF and plasma membrane proton pump inhibitors

in which the differentiation pathway is controlled by the pH of
intracellular vesicles rather than by intracellular pH itself. The model
invokes a DIF- and proton-activated vesicular chloride channel whose
opening permits acidification of the vesicles and lowers cytosolic Ca++
concn.

AN 1989:36608 CAPLUS

DN 110:36608

- TI Plasma membrane proton pump inhibition and stalk cell differentiation in Dictyostelium discoideum
- AU Gross, Julian D.; Peacey, Michael J.; Pogge von Strandmann, Ralph
- CS Dep. Biochem., Univ. Oxford, Oxford, OX1 3QU, UK
- SO Differentiation (Berlin) (1988), 38(2), 91-8 CODEN: DFFNAW; ISSN: 0301-4681
- DT Journal
- LA English
- L2 ANSWER 73 OF 74 CAPLUS COPYRIGHT 2000 ACS
- P. falciparum digestive vacuoles contg. Fe3+ oxide granules were purified ΑB from parasite homogenates by centrifugation on discontinuous sucrose gradients. Digestive vacuole membranes prepd. by osmotic lysis and washed with KCl showed no detectable contamination by erythrocyte membrane proteins and only minimal contamination by nonvacuolar parasite proteins. Purified vacuolar membranes were 2.6-fold enriched in total parasite membrane ATPase activity. This ATPase was optimally active at pH 7 in the presence of >2 mM Mg2+. Ca2+ and Mn2+ were .apprx.80-90% as effective as Mg2+, and Zn2+, Co2+, and Fe2+ also exerted some stimulatory effect. The vacuolar membrane also hydrolyzed GTP, UTP, CTP, and ADP, but AMP and 3',5'-cAMP were hydrolyzed only one-tenth as effectively as ATP. The ATPase was unaffected by vanadate, ouabain, or oligomycin but was significantly inhibited by the proton pump inhibitors NEM and NBD-Cl. Of 6 antimalarial drugs tested, quinine and quinacrine were the most effective inhibitors and mefloquine was the least effective.
- AN 1989:3408 CAPLUS
- DN 110:3408
- TI Purification of Plasmodium falciparum digestive vacuoles and partial characterization of the vacuolar membrane **ATPase**
- AU Choi, Inpyo; Mego, John L.
- CS Dep. Biol., Univ. Alabama, Tuscaloosa, AL, USA
- SO Mol. Biochem. Parasitol. (1988), 31(1), 71-8 CODEN: MBIPDP; ISSN: 0166-6851
- DT Journal
- LA English
- L2 ANSWER 74 OF 74 CAPLUS COPYRIGHT 2000 ACS
- AB A review with 43 refs. of newly developed antisecretory drugs (various substituted benzimidazoles) proton pump

 inhibitors. These inhibitors inhibit H+, K+- ATPase
 [9000-83-3] (proton pump) thereby inhibiting gastric H+ secretion. These inhibitors prevent the development of various exptl. ulcers and accelerate ulcer healing; some structure-activity relations are discussed.
- AN 1986:218442 CAPLUS
- DN 104:218442
- TI Effects of gastric **proton pump inhibitors** on gastric secretion and peptic ulcers
- AU Okabe, Susumu
- CS Dep. Appl. Pharmacol., Kyoto Coll. Pharm., Kyoto, 607, Japan
- SO Nippon Yakurigaku Zasshi (1986), 87(4), 351-60 CODEN: NYKZAU; ISSN: 0015-5691
- DT Journal; General Review
- LA Japanese

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1 WO9601624/PN
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     ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
     1996:171958 CAPLUS
     124:212082
     Multiple unit pharmaceutical preparations containing proton pump
     Bergstrand, Pontus John Arvid; Loevgren, Kurt Ingmar
     Astra Aktiebolag, Swed.
     PCT Int. Appl., 46 pp.
SO
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     English
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